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(54) Title: SELECTED RNA MOTIFS TO INCLUDE CELL DEATH AND/OR APOPTOSIS

(57) Abstract: The present application is directed to the use of dsRNA and/or ssRNA for the purpose of inducing apoptosis or cell death in proliferating cells. Specifically, low molecular weight and high molecular weight dsRNA and ssRNA are shown to induce apoptosis and/or cell death in proliferating cells, to arrest proliferation of transformed cells or tumor cells and to cause rapid induction of the cytokine TNF-alpha and/or also induce production of IL-12 which directs a Th-1 response.



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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/09261

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C12Q 1/68; A01N 43/04; C07H 21/04; A61K 31/07

US CL : 435/6, 91.1, 325, 375; 536/24.3, 24.33, 24.5; 514/44

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/6, 91.1, 325, 375; 536/24.3, 24.33, 24.5; 514/44

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	ELBASHIR et al. RNA interference is mediated by 21- and 22-nucleotide RNAs. Genes and Development, 2000 Vol. 15:188-200, see RNA synthesis and cloning of -21 nucleotide RNAs, at page 198.	28-37
X -- A	WIANNY et al. Specific interference with gene function by double-stranded RNA in early mouse development. Nature Cell Biology, 2000 Vol. 2:70-75, see RNA synthesis at page 74.	28-37 ----- 1-27
X	SVOBODA et al. Selective reduction of dormant maternal mRNAs in mouse oocytes by RNA interference. Development, 2000 Vol. 127:4147-4156, see dsRNA preparation at page 4148.	28-37
X	ZELEZNICK et al. Treatment of leukemic (L-1210) Mice with Double-stranded Polyribonucleotides. Proc Soc Exp Biol Med, 1969, Vol 130:126-128.	1-37
A	BRANCH, AD. A good antisense molecule is hard to find. TIBS, 1998 Vol. 23:45-50, see entire article.	1-27
A	JEN et al. Suppression of gene expression by targeted disruption of messenger RNA: Available options and current strategies. Stem Cells, 2000 Vol. 18:307-319, see entire article.	1-27

☒ Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents:

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"O" document referring to an oral disclosure, use, exhibition or other means

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"X"

document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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Date of the actual completion of the international search

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C. (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	OATES et al. Too much interference: Injection of double-stranded RAN has nonspecific effects in the zebrafish embryo. Developmental Biology, 2000 Vol. 224:20-28.	1-27
A	COBURN et al. siRNAs: a new wave of RNA-based therapeutics: Journal of Antimicrobial Chemotherapy, 2003 Vol. 51:753-756.	1-27
A	AGAMI, A. RNAi and related mechanisms and their potential use for therapy. Current Opinion in Chemical Biology, 2002 Vol. 6:829-834.	1-27
A	GREEN et al. Antisense Oligonucleotides: An evolving technology for the modulation of gene expression in human diseases, 2000. J Am Coll Surg Vol. 191:93-105.	1-27
A	AGRAWAL et al. Antisense therapeutics: is it as simple as complementary base recognition? Molecular Medicine Today, 2000 Vol. 61:72-80.	1-27

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Continuation of B. FIELDS SEARCHED Item 3:

CaPlus, EmBase, CancerLit, Medline, NPL, WEST

search terms: double-stranded RNA (dsRNA), single-stranded RNA (ssRNA), short interfering RNA (siRNA)